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Density of Normal Human Cerebrospinal Fluid and Tetracaine Solutions

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LEVIN, E., MURAVCHICK, S., AND GOLD, M. I.: Density of normal human cerebrospinal fluid and tetracaine solutions. Anesth Analg 1981;60:814-7.

Density and specific gravity (SG) were determined at two or more temperatures between 23 and 37 C for 15 samples of normal human cerebrospinal fluid (CSF) and CSF mixed with tetracaine, and for tetracaine solutions commonly used for spinal anesthesia. Density was determined from measured weight and volume, and SG was calculated using the density of water at the same temperature. With 95% confidence limits, SG of normal human CSF at 37 C ranges from 1.0063 to 1.0075, less variation than previously reported. Changes in temperature altered the densities of dextrose, tetracaine, and CSF, alone or in combination, in a parallel manner, but SG remained constant for each solution over the observed temperature range.

Key Words: ANESTHETIC TECHNIQUES: spinal; PHYSICS: specific gravity; TEMPERATURE: specific gravity.

THE RELIABILITY of published values (1) for the density of normal human cerebrospinal fluid (CSF) is uncertain. Many reported values are ambiguous and inconsistent due to faulty methods, inadequate standardization, or unreliable sampling. The purpose of this study was to determine precisely the density and specific gravity (SG) of normal CSF over the range 23 to 37 C and to compare them with the respective values for tetracaine and tetracaine-dextrose solutions used in clinical practice for spinal anesthesia.

Methods

Fifteen adult male patients consented to participate in a clinical study involving spinal anesthesia and elective surgery. The study was approved by the Human Studies Subcommittee, Miami Veterans Administration Medical Center. All patients were A.S.A. physical status I; none had signs, symptoms, or history of neurologic disease. A sterile 10-ml glass syringe was used to obtain a 4-ml sample of clear spontaneously flowing CSF from the lumbar subarachnoid space of each patient and was capped immediately after collection. The sample was analyzed within 30 minutes of collection using a dry, rubber-sealed pyknometer. The calibration procedure consisted of filling the pyknometer flask with distilled, demineralized water to the point of meniscus formation slightly above, and then slightly below the index mark etched on the capillary neck of the flask, and weighing each of the two volumes to the nearest 0.0001 g using a Mettler balance. Using standard tables of pure water density (2), the water volumes represented by the two meniscus positions were calculated, the difference in volume providing the calibration of the volumetric capacity of the capillary neck of the pyknometer flask. Precise observation of the meniscus of each sample with a magnified optical micrometer permitted determination of volume to the nearest 0.0001 ml. Each test solution sample was weighed on the balance and its volume measured by this technique at each of at least two or more temperatures held constant with an electric block heater and measured with a laboratory-grade mercury column thermometer. The criterion for temperature equilibration was stable meniscus formation for 2 to 3 minutes (3).

Density was calculated to the nearest 0.0001 g/ml using sample weight and sample volume measured at each temperature. Specific gravity was reported as SG x/x, the ratio of the density of the sample solution at temperature x to the density of distilled, demineral-

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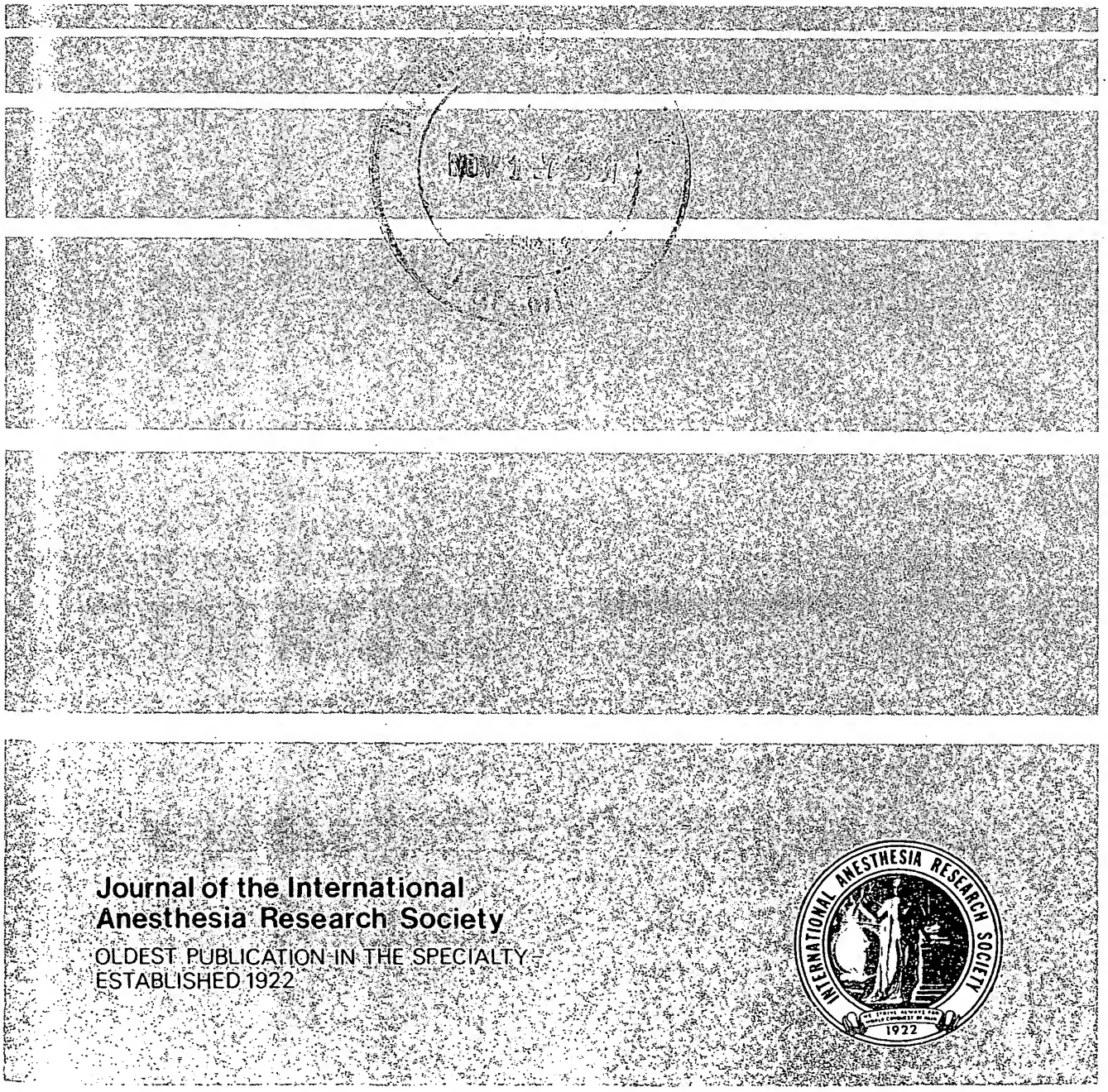

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ized water at the same temperature. Specimens included nine samples of freshly aspirated normal human CSF, six additional samples of CSF mixed with equal volumes of commercially prepared tetracaine 1% in saline, four samples of tetracaine 1% in saline, and three samples of dextrose 10% in water. In addition, three samples of tetracaine 1% in saline mixed with equal volumes of dextrose 10% were analyzed. Both drug solutions were Breon products (Breon Laboratories, New York, NY) obtained from the sealed glass ampules provided in Abbott Laboratories spinal trays, catalog #4773, obtained at random from the clinical stock in our operating room.

Mean values were compared statistically by *t*-tests. Best-fit curves were constructed from individual data points using the least-squares method.

Results

Mean density (±SD) for nine samples of normal human CSF warmed to 37 C was 1.0003 ± 0.0003 g/ml. Corresponding calculated specific gravity (SG 37/37) was 1.0069 ± 0.0003, range 1.0063 to 1.0075. The mean density of eight CSF samples which were allowed to equilibrate at room temperature (23 to 25 C) was 1.0048 ± 0.0003 g/ml, mean calculated SG of 1.0075 ± 0.0002. The relationship between CSF density and temperature over this range, illustrated in Fig 1, closely paralleled the corresponding relationship for pure water.

The density of commercially prepared isobaric, isotonic tetracaine 1% in saline warmed in vitro to 37 C was 1.0000 ± 0.0004 g/ml, corresponding to mean SG 37/37 of 1.0066 ± 0.0004, consistent with the manufacturer's data and that of other investigators (4, 5). Mean density of six samples of this tetracaine solution mixed with equal volumes of normal CSF and warmed in vitro to 37 C was 0.9998 ± 0.0002 g/ml, mean SG 37/37 of 1.0065 ± 0.0002. The differences between mean SG 37/37 of tetracaine 1%, CSF:tetracaine 1% in equal volumes, and normal human CSF were statistically insignificant ($p > 0.05$). The density-temperature relationship of these solutions obtained by repeated measurement at various temperatures is compared to that of normal CSF over the range 23 to 37 C (Fig 2).

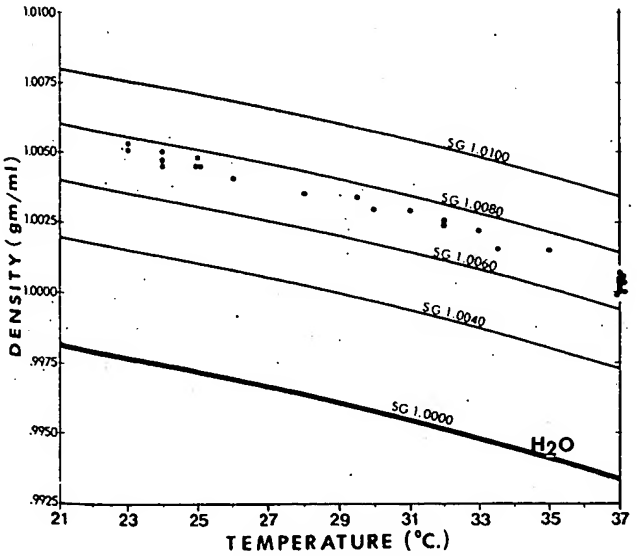

FIG 1. Temperature-density plot for 27 individual measurements using 15 samples of normal human cerebrospinal fluid. Parallel curves represent temperature-density relationships for theoretical solutions demonstrating constant specific gravity (SG) over range of temperature studied.

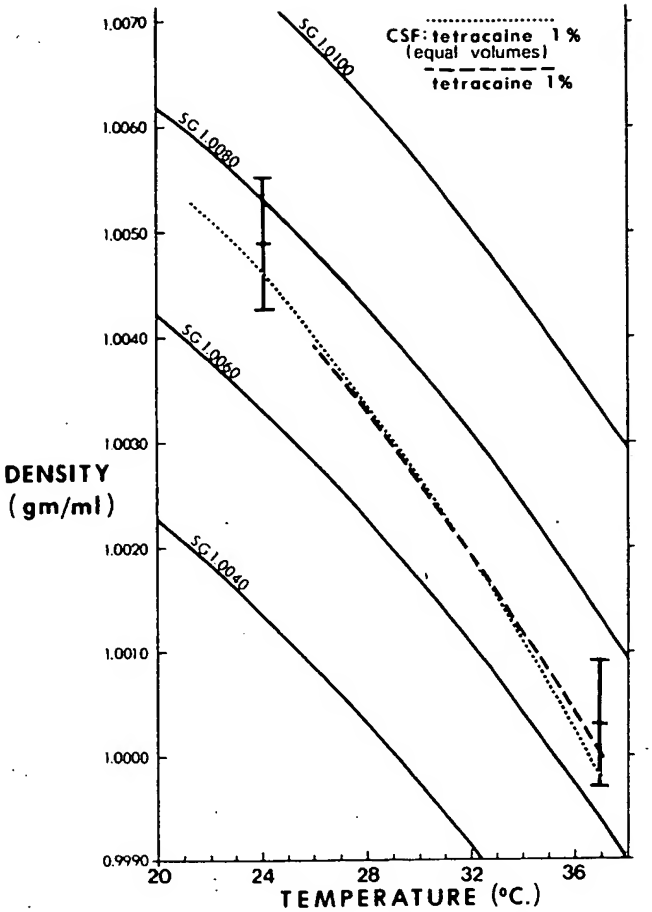

FIG 2. Best-fit curves for temperature-density relationships of tetracaine 1% in saline (n = 17, r = 0.99) and CSF:tetracaine 1%, in equal volumes (n = 14, r = 0.99). Vertical bars at 24 and 37 C represent 95% confidence limits (mean ± 2 SD) for human CSF at those temperatures.

At room temperature, the densities of aqueous dextrose 10% and dextrose 5%-tetracaine 0.5% were 1.0314 ± 0.0003 g/ml and 1.0186 ± 0.0003 g/ml, respectively. At 37 C, the mean densities of these solutions decreased to 1.0270 ± 0.0002 g/ml and

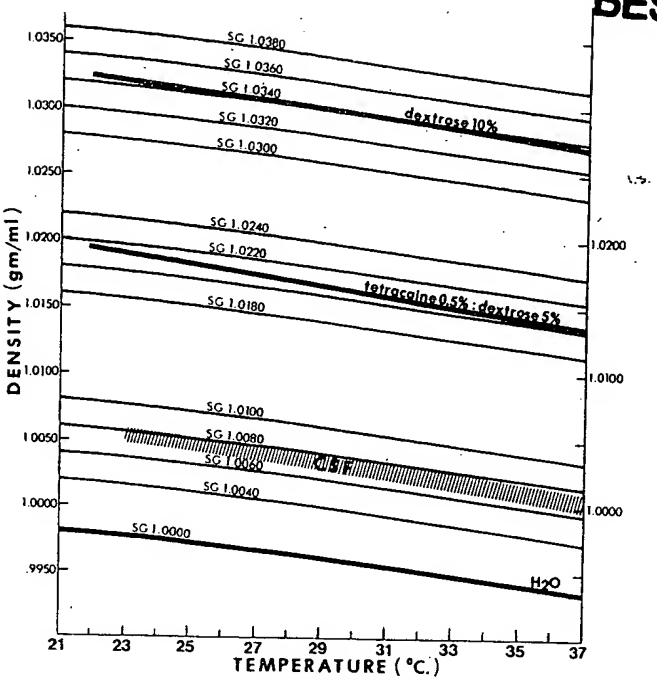

FIG 3. Best-fit curves for temperature-density relationships of aqueous dextrose 10% (n = 12, r = 0.99), tetracaine 0.5%-dextrose 5% (n = 12, r = 0.99), and 95% confidence limits (shaded area) for normal human CSF (n = 27, r = 0.99).

1.0136 ± 0.0002 g/ml, respectively, with corresponding mean SG 37/37 values of 1.0338 ± 0.0002 and 1.0202 ± 0.0003. These values were significantly greater than the corresponding values for CSF at either temperature ($p < 0.001$) (Fig 3).

Discussion

Density is a temperature-dependent physical measurement defined as the weight of a unit volume of solution at a specific temperature, and is commonly reported in units of grams per milliliter. Our results indicate that individual variation in the density of normal human CSF is far less than has been thought, with 95% confidence limits at 37 C of 0.9997 to 1.0009 g/ml. In a prior study, Davis and King (1) used a Westphal SG balance to compute densities for CSF from direct measurements of specific gravity at various temperatures and reported a density range of 0.9990 to 1.0030 g/ml at 37 C, but with CSF samples that had been collected from patients with known or suspected neurologic disease undergoing pneumoencephalography.

Specific gravity represents the ratio of the density of a solution to the density of water, and is a calculated value without units. Accurate reporting of specific gravity requires that two temperatures be stated (6): that of the solution in question (x), and that of water used as a reference solution (y), the precise format written SG x/y. Many values for the specific gravity of aqueous spinal anesthetic solutions and CSF have been reported without reference temperatures, creating confusion in terminology and prohibiting direct comparisons of data. To elucidate the behavior of our dilute aqueous solutions relative to water, we chose as our reference solution the density of water at the same temperature. Thus, in our study, y = x, and we report values as SG x/x. Our calculations for SG 37/37 of normal human CSF show a range of 1.0063 to 1.0075, less variation than the values previously reported (1).

By applying the term baric gravity to aqueous spinal anesthetic solutions, Davis and King (3) avoided the use of water as a reference standard. They defined baric gravity as the ratio of the density of a solution at 37 C to the density of CSF at 37 C. Isobaric solutions, therefore, are those with a baric gravity of unity, and hyperbaric or hypobaric solutions have baricities greater or less than unity, respectively. This concept has not been applied to clinical studies of spinal anesthesia because of uncertainty regarding the precise density of normal human CSF at 37 C, and thus baric gravity has been considered a nominal value rather than a precise calculation. Moreover, baricity as currently defined, even when precisely calculated, may be of little or no clinical utility when the temperatures of the two solutions being compared differ. Tetracaine 1% in saline has the same density as CSF at 37 C, and so is, by definition, isobaric; nevertheless, the same solution at 23 C is significantly more dense than CSF at 37 C. Therefore, unless warmed to body temperature before injection, an "isobaric" solution injected at 23 C into the subarachnoid space remains more dense than CSF until thermal equilibrium has been achieved. The kinetics of thermal equilibration of spinal anesthetics in vivo have not been studied.

Our measurements confirm that normal human CSF, like other dilute aqueous solutions (7), exhibits a curvilinear decrease in density with increasing temperature. These findings contradict the data of Davis and King (1) which show that the density of CSF is aberrant in this regard, our measurements indicating a relationship parallel to that of water, tetracaine 1% in saline, and dextrose 10% (Fig 3). The extent to which this relationship is maintained between 23 and 37 C is reflected in the relatively constant differences between the density of water, CSF, and these solutions with changing temperature.

We conclude that SG x/x for CSF varies little from one normal individual to another and remains con-

stant over the range of temperature commonly encountered in anesthetic practice. The clinical application of the concept of baric gravity awaits a more complete understanding of the kinetics of thermal equilibration within the subarachnoid space or redefinition of baricity to account for differences in temperatures of injected solutions.

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Regional Streptokinase in Myocardial Infarction

In 41 consecutive patients with an acute transmural myocardial infarction (AMI) admitted within 3 hours after the onset of symptoms the authors tried to recanalize the occluded coronary artery by an intracoronary infusion of streptokinase (SK) (2000 units/min). SK infusion was preceded by (1) an intracoronary injection of 0.5 mg of nitroglycerin to rule out coronary artery spasm, (2) an attempt to recanalize the vessel mechanically with a flexible guidewire, and (3) an intracoronary injection of plasminogen (500 units) to increase the efficacy of the subsequent SK infusion. Coronary angiography revealed a total coronary artery occlusion in 39 patients and a subtotal occlusion in two patients. In 30 patients (73%), the occluded coronary artery was successfully recanalized within 1 hour (mean 29 ± 15 minutes), resulting in prompt contrast filling of the previously occluded vessel. Nitroglycerin opened the occluded coronary artery in one patient, contrast injection in seven patients, and guidewire perforation in four of the 15 patients, in whom it was attempted. In 18 patients the occluded coronary artery was recanalized by intracoronary SK infusion alone. After the initial opening of the occluded coronary artery, subsequent SK infusion markedly reduced the degree of stenosis and visible thrombi disappeared. Clinically, recanalization was associated with significant relief of ischemic chest pain. None of the successfully recanalized patients died, including three patients with cardiogenic shock. Repeat angiography 7 to 21 days later revealed a patent coronary artery in 12 of 15 successfully recanalized patients. The left ventricular ejection fraction had significantly improved, from 37 ± 5% to 47 ± 4% (mean ± SEM). Failure of recanalization in 11 of 41 patients may be explained by the absence of coronary artery thrombosis or poor SK penetration of the thrombus because of its distal location or SK runoff into nonaffected arteries. *(Mathey DG, Kuck K-H, Tilsner V, Krebber H-J, Bleifeld W: Nonsurgical coronary artery recanalization in acute transmural myocardial infarction. Circulation 1981;63:489–97)*

(See also—Leinbach RC, Gold HK: Editorial. Regional streptokinase in myocardial infarction. Circulation 1981;63:498–9)